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Formulation, Evaluation and Stability Studies of Dutasteride Loaded Niosomal Gel

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Dutasteride, a synthetic 4-azasteroid belonging to the class of 5-α-reductase, a BCS class II drug, is used in treating Androgenetic Alopecia and Benign Prostatic Hyperplasia.
Aims: The study aims to formulate, evaluate and perform stability studies of Dutasteride-loaded topical niosomal gel.
Methodology: Formulation components such as, surfactants and cholesterol were tested for any drug/excipient interactions. Ether injection method was employed to prepare Niosomes. Five formulations were prepared and then assessed for their particle size, SEM, zeta potential, PDI, entrapment efficiency, drug content and in vitro diffusion studies. The optimized formulation F3 Consisted of Dutasteride, span 40 and cholesterol in the ratio 1:4:2. The optimized formulation (F3)

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was incorporated into a gel. Three gel formulations (FG1, FG2 and FG3) were prepared and were assessed for pH, viscosity, spreadability, drug content and in vitro diffusion studies. The optimized niosomal gel (FG2) consisted of 0.3% Optimized Niosomes and 0.75% Carbopol 934. The drug release kinetics studies were performed for the optimized gel. Finally, stability studies were performed at 30°C ± 2°C / 65% RH ± 5%.

Results: The optimized niosomes showed an Entrapment efficiency of 63.2%, zeta potential -22.7 mV, particle size 300.4 nm, drug content 86.23% and 96.23% drug release in 8 hours. The optimized niosomal gel (FG2) consisted of 0.3% Optimized Niosomes and 0.75% Carbopol 934. The gel showed pH 4.7, viscosity 66213 cps, spreadability 15.7g.cm/sec, drug content 91.4% and percent drug release 91.45% in 24 hours. The drug release kinetics studies showed that the optimized gel formulation (FG2) followed Higuchi model with R^2 value of 0.9975. The stability studies indicated that the optimized niosomal gel was stable for 90 days.

Conclusion: The stability studies confirmed the drug content and the physical nature of the gel for 90 days. Thus, the formulation can be regarded as stable and effective for drugs meant for topical application. Dutasteride gel formulations have the potential to enhance drug bioavailability by facilitating greater penetration of drugs with restricted permeability.

Keywords: Niosomal gel; dutasteride; Niosomes; androgenetic alopecia; BCS class II.

1. INTRODUCTION

The classic male pattern baldness, or androgenetic alopecia, is a thinning of the hair that often appears in middle-aged men and gets worse with age. Interestingly, independent of hereditary susceptibility, testosterone hormone plays a major role in male androgenetic alopecia.

The enzyme 5α-reductase transforms testosterone in the hair follicle cells into dihydrotestosterone (DHT). There are two forms of it: type I and type II isoenzymes. The latter seems to have a special role in male pattern baldness; it is expressed in the prostate gland and other androgen-dependent tissues, including hair follicles. Specific androgen receptors are bound by DHT. The complex that is subsequently generated penetrates the hair cell's nucleus and interacts with DNA, activating genes and causing the creation of proteins that lead to the slow transformation of normal hair follicles into "miniaturized follicles". So, this leads to shrinkage of hair follicles, shortening of the hair growth cycle, finally resulting in hair loss (Sinclair et al. 2015, Lai et al. 2012).

The two medications that are most frequently used to treat alopecia are finasteride (1mg oral dose) and dutasteride (0.5mg oral dose). These drugs inhibit type I and II 5AR enzyme, preventing the conversion of testosterone into DHT. Dutasteride therapy reduces serum DHT (98%) significantly more than does finasteride (71%) and demonstrates significantly greater improvement in hair growth compared with finasteride (Adil & Godwin 2017).

However, oral route treatment leads to significant reduction of DHT from the body and leads to serious, long lasting side effects related to fertility (Lee et al. 2019). Topical delivery of drugs would help to tackle this problem. Therefore, there is a need for targeted delivery of the drug directly to the follicles, so that the drug remains localized in the follicles and will not reach the systemic circulation (Wosicka & Cal 2010, Gu et al. 2022, Illel 1997, Lademann et al. 2007).

Vesicular drug delivery systems are designed to enhance the delivery of drugs by encapsulating them within vesicles, which are small, spherical structures composed of lipid bilayers or other materials. These systems offer several advantages over traditional drug delivery methods, making them essential in modern pharmaceutical research and applications (Alkilani et al. 2022). Advanced vesicular delivery systems like Transferosomes, ethosomes and transethosomes would enhance the delivery of drug into the systemic circulation.

Niosomes are vesicles composed of non-ionic surfactants which have demonstrated to significantly improve topical drug delivery and can also be employed in targeted drug delivery. Niosomes have been the subject of much research recently due to their potential as a vehicle for the administration of medications, antigens, hormones, and other bioactive substances. In addition, niosomes have been employed to address the issues of drug instability, insolubility, and fast degradation (Khoee & Yaghoobian 2017, Uchegbu & Florence 1995, Van Hal 1994, Schreier &

Bouwstra 1994, Mura et al. 2007). Based on various researches, Niosomes are able to deliver the drug to the deeper layers of skin, deep enough to reach the hair follicles and thus show enhanced therapeutic activity (Bhardwaj et al. 2020, Junginger et al. 1991, Verma et al. 2003, Doe et al. 2024, Liu et al. 2023). Therefore, a dutasteride loaded niosomal gel would be a promising solution to target the hair follicles and treat Alopecia.

So, the aim of this study was to incorporate the respective drug in this vesicular system and investigate the drug entrapment, drug release, drug-excipient interactions and stability studies.

2. MATERIALS AND METHODS

2.1 Materials

Dutasteride was obtained from Dr. Reddy's Laboratories Ltd., Hyderabad as a gift sample. Span 60, Span 40, Cholesterol, Carbopol, Methyl paraben were procured from s d fine-CHEM limited, Mumbai. Methanol, Potassium dihydrogen orthophosphate, Sodium hydroxide, Distilled water, Diethyl ether, Triethanolamine were procured from Thermo Fisher Scientific Pvt Ltd, Mumbai.

2.2 Methods

2.2.1 Calibration curve of pure drug Dutasteride

Dutasteride solution of concentration of 100 ug/ml was analyzed at wavelength of 220-400 nm with UV-Visible Spectrophotometer. The stock solution (100 ug/ml) was then be used to prepare serial dilutions. Sub-samples of stock solution of dutasteride were pipetted out into a succession of 25 ml volumetric flasks and volume was made up to the mark with Phosphate buffer pH 7.4. to generate the concentration ranging from 5-30 µg/mL. The absorbance of each sample was determined at 240 nm.

2.2.2 Drug excipient interaction and compatibility studies

FTIR studies were performed on the formulations to determine any drug/excipients interactions. Using the K-Br pellet method, FT-IR spectrophotometer was used to analyze the pure drug and the formulation. The analysis ranged from wave numbers 4000 to 400 cm-1 for the samples.

2.2.3 Formulation of dutasteride loaded Niosomes

Ether injection method was employed. Span and cholesterol were dissolved in (6 mL) diethyl ether, and Dutasteride 50mg was dissolved in (6 mL) methanol, then both the solutions were mixed together. 50 mL of phosphate buffer solution (pH 7.4) was kept at 61-66°C and the previously prepared solution was administered at a rate of 1mL/min into this buffer solution by using a syringe and the solution was constantly stirred. After the solution was gradually introduced into the aqueous phase, temperature variations between the phases rapidly evaporated the ether, which led to immediate vesiculation and niosomes creation (Prem Kumar et al. 2013, Masjedi & Montahaei 2021, Abdelkader et al. 2014, Manosroi et al. 2003). The formed niosomal suspension was sonicated for 2 min. The niosomal suspension was left overnight at 3-5°C before being refrigerated for future study.

2.2.4 Characterization and evaluation of dutasteride loaded Niosomes

2.2.4.1 Vesicle morphology

The Form and structure of the drug loaded niosomal formulations was ascertained by Scanning Electron Microscopy (HITACHI) (Prem Kumar et al. 2013, Masjedi & Montahaei 2021, Bhaskaran & Lakshmi 2009).

Table 1. Formulation table of Dutasteride Niosomes

Formulation	Drug (mg)	Span 60 (mg)	Span 40 (mg)	Cholesterol (mg)	Drug/Surfactant/cholesterol ratio
F1	50	200	-	100	1:4:2
F2	50	100	-	100	1:2:2
F3	50	-	200	100	1:4:2
F4	50	-	100	100	1:2:2
F5	50	100	100	100	1:4:2

2.2.4.2 Particle size, PDI and Zeta potential

Using Nano particle Analyzer (HORIBA SCIENTIFIC) to determine the average particle length, polydispersity index (PDI) and Zeta potential (Prem Kumar et al. 2013, Abdelkader et al. 2014, Manosroi et al. 2003).

2.2.4.3 Drug entrapment efficiently

The entrapment efficiency of niosomes was calculated with the usage of cooling centrifuge. The prepared formulations were put through the centrifugation at 17,000 rpm for at 4°C for 30 mins. After the supernatant was decanted, the amount of free drug was examined by UV/visible spectrophotometer at λmax of 240 nm Prem Kumar et al. 2013, Masjedi & Montahaei 2021, Abdelkader et al. 2014). The following formula was then used:

%Drug entrapment = (Total drug - Drug in supernatant / Total drug) x 100

2.2.4.4 Drug content

To determine the extent of dutasteride present in the niosomes, UV-visible spectrophotometer was used. In 10 mL methanol, Niosomes (100 mg) were dissolved by shaking for 5 mins. A mL from this solution was taken and made up to 10 mL with methanol. After that, sub samples were taken out, and absorbance was recorded at the appropriate wavelength (Masjedi & Montahaei 2021, Abdelkader et al. 2014, Manosroi et al. 2003).

2.2.4.5 In vitro diffusion studies

Franz-diffusion cell was used for this purpose. 10 ml of the prepared formulation was taken in the donor compartment and it was separated from the receptor compartment that was filled with phosphate buffer pH 7.4 by a membrane. A magnetic stirrer was used to agitate the medium at room temperature at 100 rpm. Samples were withdrawn and fresh buffer solution was added regularly at pre-decided time intervals. The collected samples after suitable dilution were analyzed spectrophotometrically at 240 nm ((Prem Kumar et al. 2013, Bhaskaran & Lakshmi 2009)

2.2.5 Formulation of niosomal gel of Dutasteride

The Carbopol 934 concentrations (0.75%, 1%) were used to optimize the niosomal gel. Distilled water was used to disperse the polymer. The mixture was then continued to be stirred until it thickened. Following full dispersion, triethanolamine and methyl paraben were added. The polymer gel was combined with required quantity of the optimized niosomal dispersion while being constantly stirred. A sufficient amount of distilled water was added to get the required quantity of gel. A plain gel was also created for comparison study (Smith et al. 2024, Doe et al. 2024, Sravan et al. 2022).

2.2.6 Characterization and evaluation of Dutasteride Loaded Niosomal gel

2.2.6.1 Physical appearance

The visual characteristics of every prepared gel formulation, including transparency, color, texture, stickiness, greasiness, smoothness, stiffness was determined (Smith et al. 2024, Doe et al. 2024, Sravan et al. 2022).

2.2.6.2 Homogeneity

By visual checking, the uniformity of the Dutasteride Niosomal gels was verified (Smith et al. 2024, Doe et al. 2024, Sravan et al. 2022).

2.2.6.3 Viscosity study of gels

Niosomal gels were evaluated for their viscosity by Brookfield viscometer (DV-E, HA 22) (Smith et al. 2024, Doe et al. 2024, Sravan et al. 2022).

Table 2. Formulation table for 0.3% Dutasteride in 10gm Niosomal gel

Ingredients	Formulation 1 (Fg1)	Formulation 2 (Fg2)	Formulation 3 (Fg3)
F3 optimized niosomes	-	0.3%	0.3%
Pure Dutasteride	0.3%	-	-
Carbopol 934	0.75%	0.75%	1%
Methyl Paraben	0.15%	0.15%	0.15%
Triethanolamine	q.s	q.s	q.s
Distilled Water	Up to 100ml	Up to 100ml	Up to 100ml

2.2.6.4 pH measurement

A digital pH meter was used. Before proceeding, the pH meter was calibrated (Doe et al. 2024, Sravan et al. 2022)

2.2.6.5 Spreadability

Good amount of sample was placed in between two glass slides and was squeezed to a consistent thickness by keeping one kg weight over it for 5 min (Smith et al. 2024). The formula:

> Spreadability = (Weight applied to the upper slide / Length moved on the glass) / Time

2.2.6.6 Drug content

1 gm of the gel was combined with 100 ml of methanol. The stock solution was filtered and sub samples of different concentrations were made with appropriate dilutions and then analyzed at 240 nm. Drug content was determined (Smith et al. 2024, Doe et al. 2024, Sravan et al. 2022).

2.2.6.7 In vitro diffusion studies

The permeation investigation was carried out in phosphate-buffered saline pH 7.4, that was sustained at 37 ± 0.2°C in a Franz diffusion cell (FDC). The stirring speed of the diffusion medium was kept at 100 ± 4 rpm. The membrane, which serves as a diffusion barrier between the donor and receptor compartments, was attached in the base of the FDC donor compartment. Formulation (10 ml) was kept in the donor compartment, and the study was continued for 8 h. The sample (1 ml) was taken out at pre-decided time intervals and the removed volume was replaced with fresh buffer. After passing through a 0.20-µm membrane filter, the extracted samples were examined (Smith et al. 2024, Doe et al. 2024)

2.2.6.8 Drug Release kinetics studies

Various release models like zero order, first order, Higuchi-equation, and Peppas-Korsemeyer were fitted to Niosomal gel formulation to ensure the drug release mechanism.

2.2.7 Stability studies

In accordance with ICH requirements, the stability analysis of the Niosomal gels was conducted. Freshly made formulations were separated into groups and stored at 30°C ± 2°C / 65% RH ± 5%. for 90 days. During various time intervals, samples were taken out and various parameters were evaluated (Doe et al. 2024).

3. RESULTS AND DISCUSSION

3.1 Results

3.1.1 Calibration curve results

The calibration curve of the dutasteride was developed by dissolving in methanol for stock solution and made dilutions with phosphate buffer pH 7.4. The standard dutasteride graph demonstrated strong linearity, with R^2 = 0.9989, signifying its adherence to the “Beer-Lambert” law.

3.1.2 Drug and excipient compatibility studies

The functional groups in FT-IR spectrum of pure drug and formulation were almost similar and didn’t show any interactions and thus proves its compatibility.

In conclusion, the functional groups in FT-IR spectrum of pure drug and formulation were almost similar and thus proves its compatibility.

3.1.3 Characterization and evaluation results of dutasteride Niosomes

The Prepared Niosomes were characterized for various physicochemical properties.

Table 3 gives the results.

3.1.3.1 In-vitro diffusion studies

Niosomes F3- formulation showed the appropriate particle size of 300.4nm, PDI of 302, zeta potential value of -22.7, % entrapment efficiency 63.2% and drug content was 86.23% and showed highest drug release across the membrane 96.23%. Hence it was selected as optimized formulation.

3.1.3.2 Scanning electron microscopy evaluation and zeta potential

The optimized Niosomal formulation F3 was subjected to SEM analysis for describing the niosomes dimensions and form. Microscopic assessment showed, spherical Uni-lamellar vesicles size.

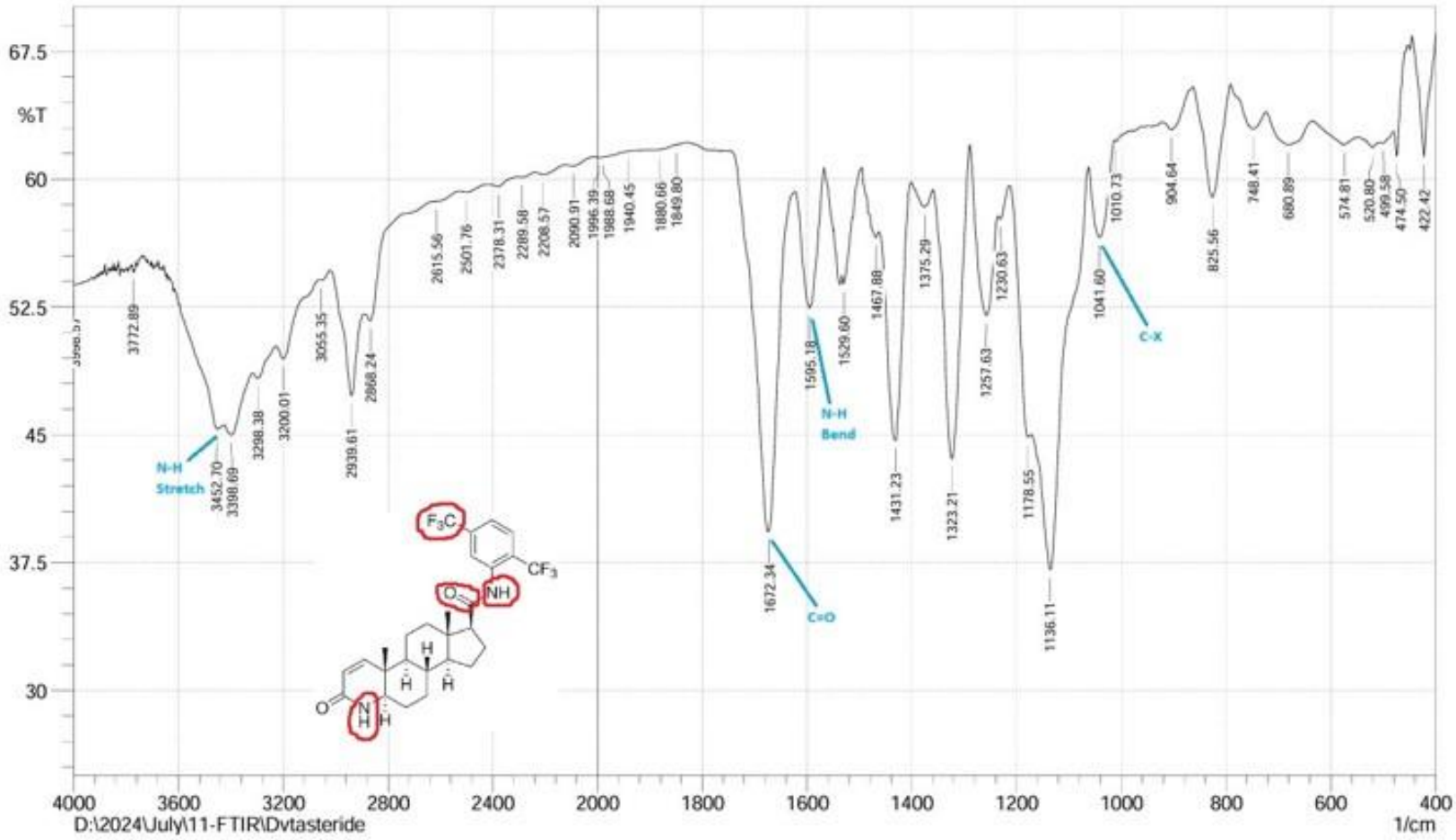

Fig. 1. FTIR Spectrum of pure Dutasteride

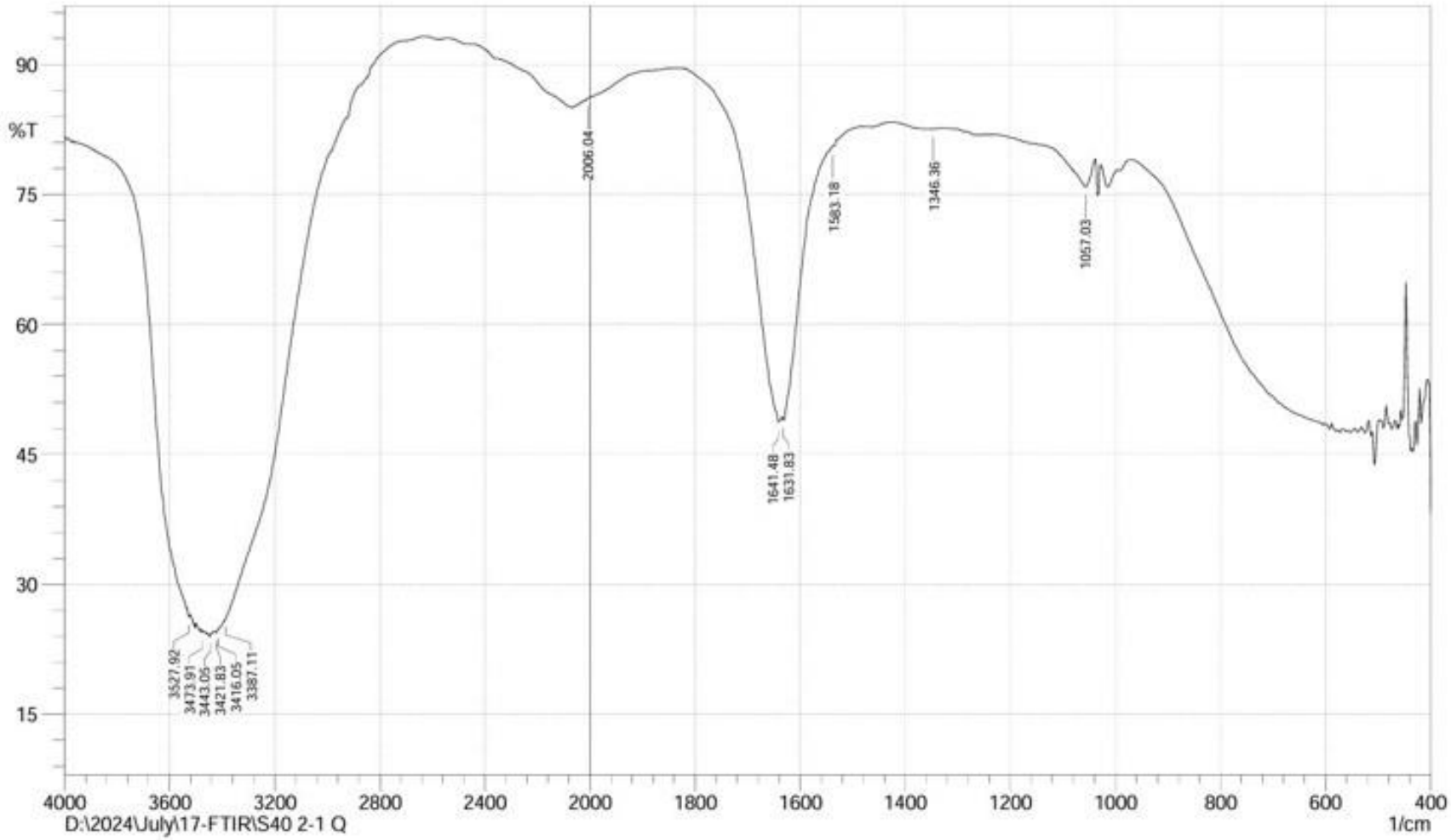

Fig. 2. FTIR spectrum of optimized formulation i.e., Dutasteride + Span 40 + Cholesterol

Table 3. FTIR Results of Pure Drug and optimized Formulation

Groups	Pure Drug	Formulation
N-H stretch	3452.70 cm-1	3443.05 cm-1
N-H bend	1595.18 cm-1	1583.18 cm-1
C=O stretch	1672.34 cm-1	1641.48 cm-1
C-F or C-X	1041.60 cm-1	1057.03 cm-1

Table 4. Characterization and evaluation results of all dutasteride Niosomal formulations

Formulation	Particle size (nm)	PDI	Zeta Potential (mV)	Entrapment efficiency (%)	Drug Content (%)
F1	290.3 ± 2.03	0.381	-20.5	59.8%	84.5
F2	140.8 ± 2.21	0.224	-19.1	53.6%	80.18%
F3	300.4 ± 2.38	0.302	-22.7	63.2%	86.23%
F4	152 ± 2.13	0.258	-15.6	51.1%	81.42%
F5	257.7 ± 2.23	0.318	-21.3	57.4%	83.28

Table 5. *In vitro* diffusion studies results of F1-F5 Niosomal formulations

Time (Hour)	F1 (% released)	F2 (% Released)	F3 (% Released)	F4 (% Released)	F5 (% Released)
0	0	0	0	0	0
1	34.14 ± 0.89	37.45 ± 0.18	45.14 ± 0.17	32.18 ± 0.20	40.15 ± 0.57
2	45.01 ± 0.17	44.18 ± 0.33	58.77 ± 0.23	43.01 ± 0.76	52.89 ± 0.54
3	52.33 ± 0.24	53.68 ± 0.85	71.52 ± 0.45	52.54 ± 0.13	64.19 ± 0.33
4	63.75 ± 0.41	58.82 ± 0.47	76.17 ± 0.68	58.21 ± 0.47	72.56 ± 0.75
5	72.41 ± 0.54	62.32 ± 0.31	79.28 ± 0.22	62.68 ± 0.51	76.84 ± 0.55
6	78.22 ± 1.22	67.59 ± 0.43	84.35 ± 0.13	66.48 ± 0.38	81.11 ± 0.24
7	83.08 ± 1.43	73.22 ± 0.93	92.11 ± 0.09	71.18 ± 0.18	84.80 ± 1.78
8	94.17 ± 1.69	85.85 ± 0.67	96.23 ± 0.34	78.50 ± 0.56	90.02 ± 1.47

**Average of three values*
± Standard deviation

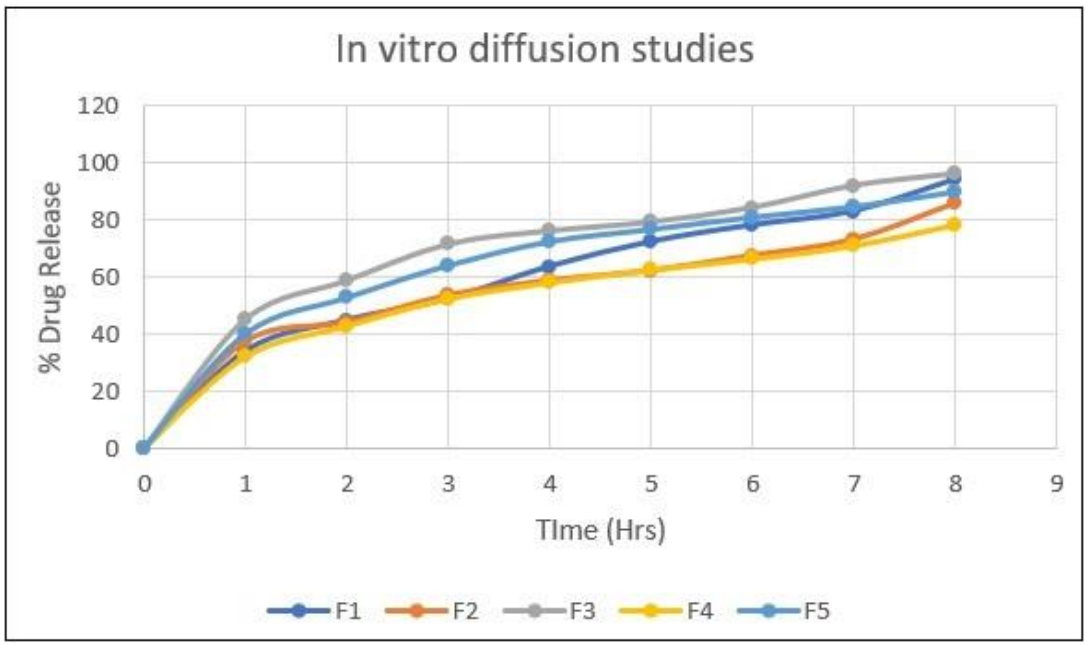

Fig. 3. *In vitro* diffusion studies of all niosomal formulations

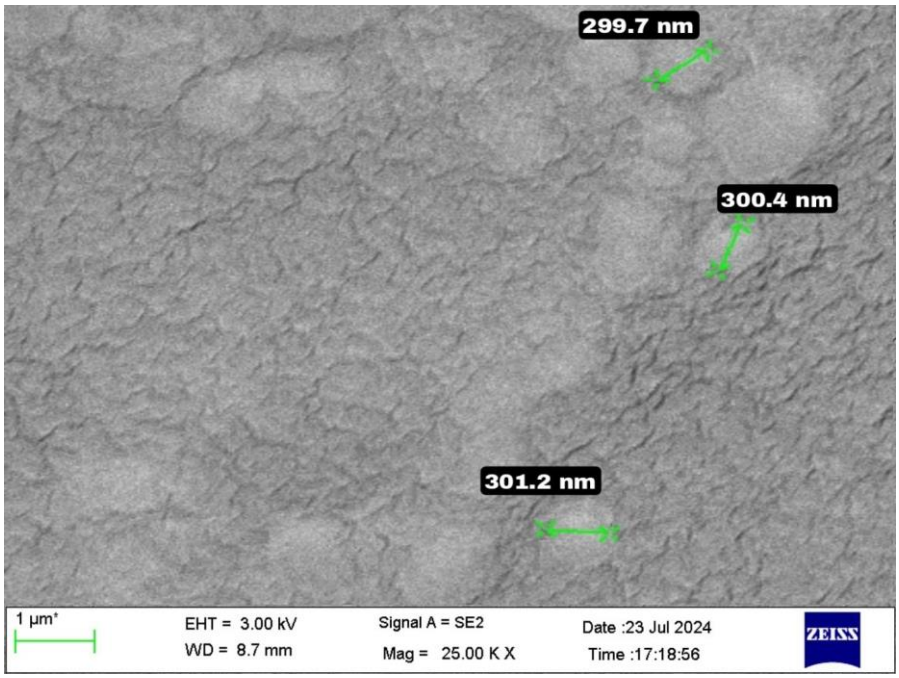

Fig. 4. SEM Pic of F3 formulation

Measurement Results

Date	: 12 July 2024 14:30:06
Measurement Type	: Particle Size
Sample Name	: S40 2-1 Q-SIZE
Scattering Angle	: 173
Temperature of the holder	: 25.0 deg. C
T% before meas.	: 81
Viscosity of the dispersion medium	: 0.895 mPa.s
Form Of Distribution	: |Standard|
Representation of result	: Scattering Light Intensity
Count rate	: 2568 kCPS

Calculation Results

Peak No.	S.P.Area Ratio	Mean	S. D.	Mode
1	1.00	226.7 nm	59.2 nm	206.6 nm
2	---	--- nm	--- nm	--- nm
3	---	--- nm	--- nm	--- nm
Total	1.00	226.7 nm	59.2 nm	206.6 nm

Histogram Operations

Size (Median)	: 217.9 nm
Mode	: 206.6 nm
% Cumulative (1)	: 5.0 (%) - 144.2 (nm)
% Cumulative (2)	: 10.0 (%) - 156.0 (nm)
% Cumulative (3)	: 20.0 (%) - 173.3 (nm)
% Cumulative (4)	: 30.0 (%) - 187.9 (nm)
% Cumulative (5)	: 40.0 (%) - 202.6 (nm)
% Cumulative (6)	: 50.0 (%) - 217.9 (nm)
% Cumulative (7)	: 60.0 (%) - 234.8 (nm)
% Cumulative (8)	: 70.0 (%) - 254.0 (nm)
% Cumulative (9)	: 80.0 (%) - 277.0 (nm)
% Cumulative (10)	: 90.0 (%) - 310.7 (nm)

Cumulant Operations

Z-Average	: 300.4 nm
PI	: 0.302

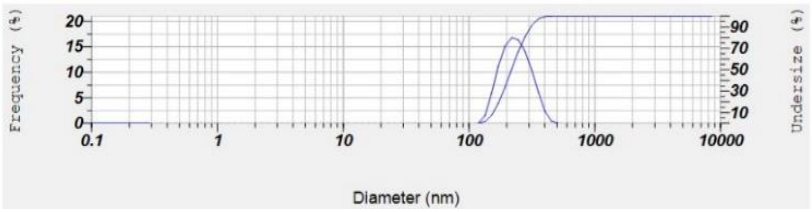

Fig. 5. Particle size and PDI of F3 Formulation

Measurement Results

Date	: 11 July 2024 17:02:23
Measurement Type	: Zeta Potential
Sample Name	: S40 2-1 Q-ZETA
Temperature of the holder	: 25.0 deg. C
Viscosity of the dispersion medium	: 0.894 mPa.s
Conductivity	: 0.425 mS/cm
Electrode Voltage	: 3.3 V

Calculation Results

Peak No.	Zeta Potential	Electrophoretic Mobility
1	-2.2 mV	-0.000017 cm2/Vs
2	-41.8 mV	-0.000324 cm2/Vs
3	--- mV	--- cm2/Vs

Zeta Potential (Mean)	: -22.7 mV
Electrophoretic Mobility mean	: -0.000176 cm^2/Vs

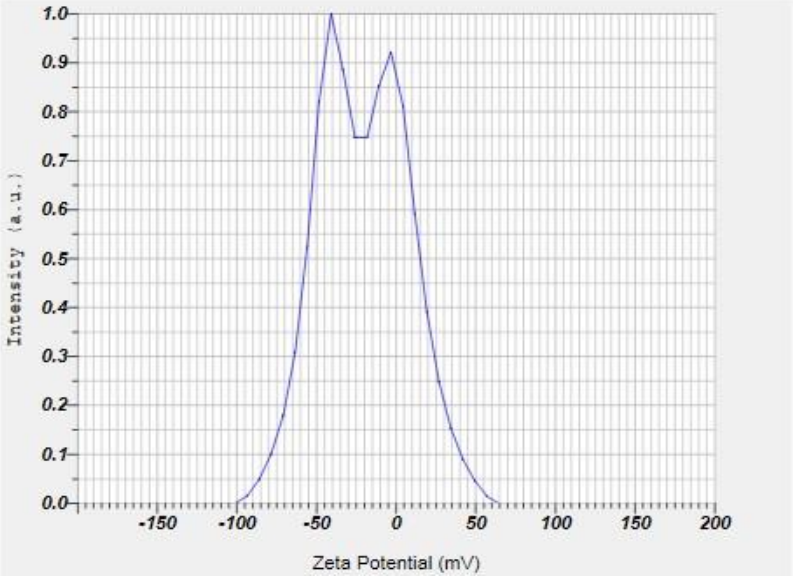

Fig. 6. Zeta potential value of F3 Formulation

3.1.4 Characterization and evaluation results of the prepared dutasteride Niosomal Gels

Table 6. Evaluation parameters of gels

Formulation	pH	Viscosity (cp)	Homogeneity	Spreadability (g.cm/sec)	Drug content (%)
FG1 or Plain gel 0.75%	4.3	67175	Good	15.9	85.5
FG2 or 0.75% optimized gel	4.7	66213	Good	15.7	91.4
FG3 or 1% gel	5.2	65987	Good	15.57	88.6

3.1.4.1 In-vitro diffusion study

FG2 gel formulation showed maximum drug release (91.45 %), good homogeneity, maximum drug content, good viscosity and pH. As a result, it was regarded as the optimal gel formulation.

Table 7. *In vitro* diffusion studies of niosomal gels

Time (hrs)	FG1 (% released)	FG2 (% released)	FG3 (% released)
0	0	0	0
1	3.87	16.76	9.21
2	7.38	24.38	14.38
4	10.23	33.74	20.74
6	15.28	42.23	28.83
8	20.43	50.28	35.28
24	57.55	91.45	82.45

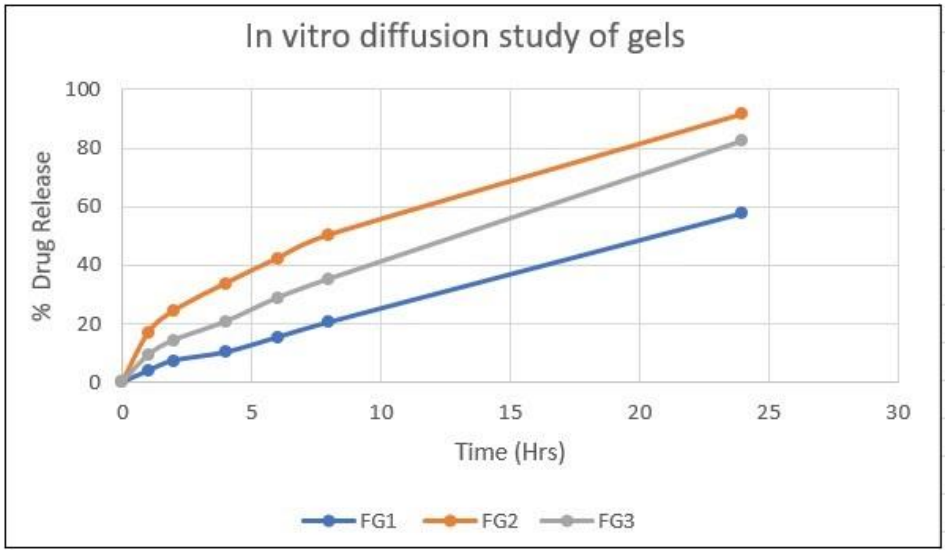

Fig. 7. *In vitro* diffusion studies of all niosomal gels

3.1.4.2 Drug release kinetic studies

Table 8. Regression (R^2) values of various pharmacokinetic profiles of the optimized gel formulation (FG2)

Zero order	First order	Korsmeyer-Peppas	Higuchi
0.922	0.9882	0.9921	0.9975

The drug release kinetics and Release mechanism were applied to the prepared 0.75% Carbopol Niosomal gel (FG2) or the optimized gel. The drug release time profile was fitted to the formulations using a variety of equations, including Zero order, First order, Korsmeyer-Papas and Higuchi. The drug release kinetics showed that the gel followed Higuchi model (R^2 = 0.9975).

3.1.5 Stability studies

Table 9. Stability studies of the optimized gel (FG2)

Formulation	FG2			
Storage Condition	30°C ± 2°C / 65% RH ± 5%			
Time Intervals (Days)	**0**	**30**	**60**	**90**
pH	4.7	4.6	4.6	4.5
Viscosity (cP)	66213	65734	64345	63515
Spreadability	15.7	15.4	15.3	15.2
Drug Content Uniformity (%)	91.4	91.2	91.1	90.9

The stability study of the niosomal gel was performed as per ICH guidelines. The gel's physical form, pH, viscosity, homogeneity and drug content was good during the period of storage. This shows the stability of the gel formulation.

3.2 Discussion

As of now, no work has been done on Niosomal Gel of dutasteride. So, this is an attempt to incorporate the respective drug in this vesicular system.

The FTIR Studies indicated that there were no drug-excipient interactions.

Among the 5 niosomal formulations F3 was selected as optimized formulation.

The particle size of Optimized formulation was 300.4nm. Based on the previous study of follicular targeting assessment of tretinoin and bicalutamide loaded niosomes, the particles of size around 300nm can easily penetrate through the skin barrier and reach the hair follicles.

Also, in the optimized formulation, the span concentration was double than that of cholesterol. Increase in the span concentration and a decrease in cholesterol concentration increases the vesicle size and entrapment efficiency based on the previous study of Development and characterization of niosomal gel of fusidic acid.

And it showed the highest drug release.

And the 0.75% niosomal gel showed good viscosity, Spreadability and drug release compared to the plain gel and 1% niosomal gel. This could be due to low Carbopol concentration of 0.75% compared to 1%. and Hence it was selected as optimized gel.

So, this was the rationale for deciding the optimized dutasteride niosomal gel formulation, as it could readily reach the hair follicles and provide a sustained action and hence could be used for treating androgenetic alopecia.

Stability studies indicated the stability of the gel for 90 days This can be attributed to the use of double the span concentration than that of cholesterol which increases the electrostatic repulsion between the vesicles and decreases particle aggregation.

4. CONCLUSION

The current study's objective was to prepare, characterize and evaluate niosomal gel loaded with Dutasteride. According to pre-formulation research studies, Dutasteride was soluble in Methanol. Furthermore, FTIR analysis showed that the drug and the excipients showed no interactions. Among the 5 formulations of niosomes prepared, the F3 formulation prepared with the drug, span 40 and cholesterol in 1:4:2 ratio was the optimized formulation, with an In vitro release of approximately 96.23% within 8 hours, 86.23% drug content, entrapment efficiency of 63.2%, -22mV zeta potential, and a particle size of 300.4 nm. SEM analysis of optimized dutasteride niosomes revealed spherical, unilamellar vesicles. The optimized niosomes (F3) were incorporated into three gel formulations. Consequently, the optimized niosomal gel (FG2) had a pH of 4.7, viscosity 66213 cps, spreadability 15.7 g.cm/sec, 91.4% drug content and 91.45% drug release in 24 hours. The drug release kinetics showed that the gel followed Higuchi model. The stability studies confirmed the drug content and the physical nature of the gel for 90 days. Thus, the formulation can be regarded as stable and effective for drugs meant for topical application. Dutasteride gel formulations have the potential to enhance drug bioavailability by facilitating greater penetration of drugs with restricted permeability.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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